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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,786	11/08/2000	Sudhir Agrawal	47508.700	2469

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/708,786	**Applicant(s)** AGRAWAL, SUDHIR	
	Examiner Terra C. Gibbs	**Art Unit** 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,2,5,6,8-11,14,15,17-20,23,24 and 26-37*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

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Continuation of 3. NOTE: The proposed amendment will not be entered because it would necessarily require new search and further consideration. The claims have been amended to include a specific statistical significance numeration (p value) and a specific nucleotide length. These new limitations would potentially raise new art issues not previously considered since said specific statistical significance numeration (p value) and nucleotide length have not been recited in any claims examined heretofore. Further, the new limitation reciting "that is from about 5 to about 100 nucleotides in length" appears to be new matter. In Applicants Remarks filed June 6, 2005, Applicants contend that support for the new limitation "that is from about 5 to about 100 nucleotides in length" can be found in the instant specification at page 8, lines 23-27. Referring to Applicants specification at page 8, lines 23-27, Applicants disclose preferred embodiments of oligonucleotide lengths including from about 13 to about 100, about 15 to about 50, about 15 to about 35, and about 5 to about 15. However, these embodiments do not support the specific limitation "about 5 to about 100". In summary, since the new limitations reciting a specific statistical significance numeration (p value) and a specific nucleotide length are new limitations never examined heretofore, and since the limitation "that is from about 5 to about 100 nucleotides in length" appears to be new matter, the proposed amendment will not be entered because it would necessarily require new search and further consideration and potentially raise new issues not previously considered.

Continuation of 5. Applicant's reply has overcome the following rejection(s): If entered, Applicant's reply would overcome the 35 U.S.C. 112, second paragraph rejection against claims 1,2,5,6,8-11,14,15,17-20,23,24 and 26-37 for being indefinite. This rejection would be withdrawn in view of Applicants amendment to the claims to recite a specific statistical significance (p value). If entered, Applicants reply would overcome the 35 U.S.C. 102(b) rejection against claims 1, 2, 5, 10, 11, 14, 19, 20, and 23 as being anticipated by Koike et al. (1997). This rejection would be withdrawn in view of Applicants amendment to the claims to recite "that is from about 5 to about 100 nucleotides in length". It is noted that Koike et al. teach an antisense transcript that is approximately 800 nucleotides long. However, it is noted that if entered, the new limitation, "that is from about 5 to about 100 nucleotides in length" appears to be new matter as discussed in #3 above. It is further noted that in response to this rejection, Applicants argue that the term "oligonucleotide" is known in the art to encompass only relatively short polynucleotide chains and thus the 805 antisense transcript taught by Koike et al. does not anticipate the oligonucleotide used in the instant method. Applicants have supported this argument with Exhibit A, a Merriam Webster's Medical Desk Dictinary definition for the term "oligonucleotide". The Webster's Dictionary definition recites, "oligonucleotide - a relatively short single-stranded nucleic-acid chain, usually consisting of up to approximately 20 nucleotides". This definition renders the claim very broad since there is no absolute or end limit to the term "oligonucleotide" since it is "relatively short" or usually "up to approximately 20 nucleotides". In this regard there is no end limit term "oligonucleotide" and therefore, in the Examiner's eyes, the approximate 805 nucleotide long antisense transcript taught by Koike et al. is a relatively short single-stranded nucleic-acid chain. In summary, the 35 U.S.C. 102(b) rejection against claims 1, 2, 5, 10, 11, 14, 19, 20, and 23 as being anticipated by Koike et al. (1997) is withdrawn in view of Applicants amendments to the claims. However, Applicants amendments to the claims appears to be new matter as discussed in #3 above. It is noted that Applicants arguments and Exhibit A regarding the definition and interpretation of the term "oligonucleotide" did not persuade the Examiner to withdraw this rejection.

If entered, Applicant's reply would overcome the 35 U.S.C. 103(a) rejection against claims 1-6, 8-15, 17-24, 26, 27, and 29-34 as being unpatentable over Koike et al. (Cancer Research, 1997 Vol. 57:5475-5479) in view of Baracchini et al. [U.S. Patent No. 5,801,154]. This rejection would be withdrawn in view of Applicants amendment to the claims to recite "that is from about 5 to about 100 nucleotides in length". It is noted that Koike et al. teach an antisense transcript that is approximately 800 nucleotides long. However, it is noted that if entered, the new limitation, "that is from about 5 to about 100 nucleotides in length" appears to be new matter as discussed in #3 above. It is further noted that in response to this rejection, Applicants argue that the claimed invention as a whole, including inherent properties be considered. Applicants rely on MPEP 2141.02. Applicants contend that there would have been no motivation to modify the gene-specific antsiense cMOAT transcript taught by Koike et al. to arrive at the inherently sequence-independent oligonucleotides of the claimed invention. Applicants argue that the instant specification utilizes oligonucleotides of no particular sequence and there is no motivation to modify the teachings of Koike et al. because one of skill in the art would have considered oligonucleotides that were nonspecific to endogenous host target genes to be biologically ineffective in the claimed co-treatment method. This argument has been considered but is not found persuasive because the claims utilize an oligonucleotide that is from about 5 to about 100 nucleotides in length, wherein the oligonucletoide does not have two 5' and four 3' 2-O-methylribonucleosides or the sequence of SEQ ID NO:1. The claims do not require that the oligonucleotide be nonspecific to an endogenous target gene. Therefore, the claims are broadly drawn to any oligonucleotide, sequence dependent or otherwise, so long as it is from about 5 to about 100 nucleotides in length, does not have two 5' and four 3' 2-O-methylribonucleosides or the sequence of SEQ ID NO:1. Applicants also argue that while the instant claims allow for sequence independent oligonucleotides but do not specifically require that the oligonucleotide are necessarily non-targeting, the sequence independent is relevant to the assessment of the claimed invention as a whole. This argument has been considered, but is not found persuasive because for prior art purposes, the claims are given their broadest reasonable interpretation. Broadly interpreted, the claims utilize any oligonucleotide, so long as it is from about 5 to about 100 nucleotides in length, does not have two 5' and four 3' 2-O-methylribonucleosides or the sequence of SEQ ID NO:1. If a teaching meets the structural limitations of the claim, then it constitutes prior art and has no inventive distance from that which is recited in the instant specification. While the Examiner agrees that the sequence independence is relevant to the assessment of the claimed invention as a whole, the claims are broadly drawn to utilizing any oligonucleotide, so long as it is from about 5 to about 100 nucleotides in length, does not have two 5' and four 3' 2-O-methylribonucleosides or the sequence of SEQ ID NO:1. In this regard, the sequence independent is irrelevant to the assessment of the claimed invention as a whole when analyzed in light of broadly drawn claims. In summary, the 103(a) rejection against claims 1-6, 8-15, 17-24, 26, 27, and 29-34 as being unpatentable over Koike et al. (Cancer Research, 1997 Vol. 57:5475-5479) in view of Baracchini et al. [U.S. Patent No. 5,801,154 is withdrawn in view of Applicants amendments to the claims. However, Applicants amendments to the claims appears to be new matter as discussed in #3 above. It is noted that Applicants arguments regarding this rejection did not persuade the Examiner to withdraw this rejection since the claims are broadly drawn to utilize any oligonucleotide, so long as it is from about 5 to about 100 nucleotides in length, does not have two 5' and four 3' 2-O-methylribonucleosides or the sequence of SEQ ID NO:1. The claims encompasses both sequence dependent and independent oligonucleotides and thus one of ordinary skill in the art would have been motivated to modify the oligonucleotide.

If entered, Applicant's reply would overcome the 35 U.S.C. 112, first paragraph rejection against claims 1, 10, 19, and 35-37 as failing to comply with the written description requirement. This rejection would be withdrawn in view of Applicants amendment to the claims to remove the term "CPT-11 analog".

Continuation of 11. does NOT place the application in condition for allowance because: The request addresses the claims as amended, however the claims as amended have not been considered on the record.